

The University of Chicago

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REAGENTS

THE ACTION OF ISOBUTYL MAGNESIUM
BROMIDE ON KETONES

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

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ALICE H. TANNER

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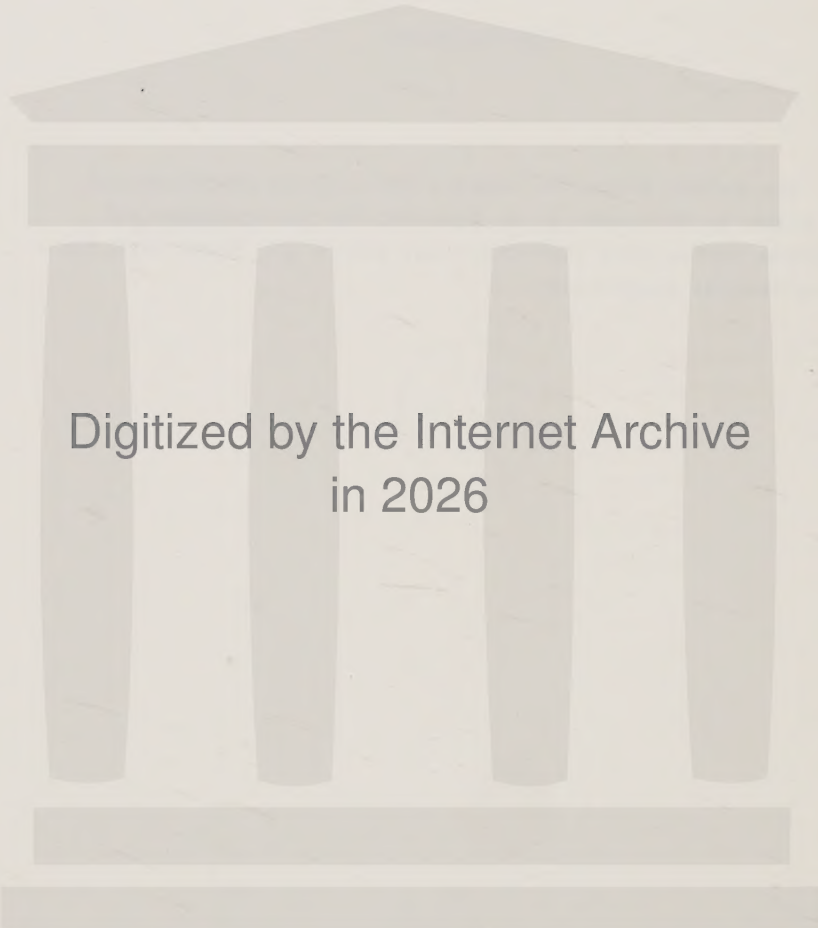
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INTRODUCTION

There has been considerable interest evinced in the reducing action of Grignard reagents, and although many observations have been made and several theories advanced concerning the mechanism, until recently little progress has been made toward a correlation of the structure of the reagents involved and the reducing activity. The problem of the reduction of ketones by Grignard reagents, to which this investigation is limited, resolves itself into the relationship between the amount of reduction and the Grignard reagent, and secondly, the influence of the structure of the ketone upon the amount of reduction. The first part of the problem was investigated by Kharasch and Weinhouse,¹ who made an exhaustive study of the reduction of benzophenone by Grignard reagents. The object of the present investigation is to attack the problem from the second point of view, which involves the determination of the amount of reduction of a series of ketones by a single Grignard reagent.

¹M. S. Kharasch and S. Weinhouse, J. Org. Chem., 1, 209 (1936).

HISTORY

Investigations of the reducing action of Grignard reagents on ketones have been largely limited to the effect of the reagent itself. Only a few studies of the action of a single Grignard reagent on a number of related ketones have been made, and of these studies none is entirely satisfactory for determining the part played by the ketone. The work of Stas,² Conant and coworkers,³ and Blatt and Stone⁴ dealt with aliphatic ketones, which, as was pointed out by Blicke and Powers,⁵ are not suitable for this purpose because of their ability to react in the enolic form with alkyl magnesium halides. The results of Blicke and Powers, which were obtained from the study of a number of closely related ketones, are not conclusive: the amount of reduction was determined by the isolation of the products, a method which they admit is not quantitative because of the closely related solubilities and mutual solubilities of the products; the Grignard solutions were not filtered, a matter of some importance as was pointed out by Kharasch and Weinhouse;⁶ and the amount of reduction was calculated on the basis of the ketone added and not on the basis of the amount of ketone which reacted, a procedure which can lead to erroneous conclusions, since the velocities of the different reactions may vary widely.

The theories advanced concerning the mechanism of the reaction have been concerned chiefly with the part played by the Grignard reagent. Hess and Rheinbolt⁷ have postulated the formation of an intermediate addition complex which may either rearrange to give the normal addition product or may lose an unsatu-

²J. Stas, Bull. soc. chim. Belg., **34**, 188 (1925).

³J. B. Conant and A. H. Blatt, J. Am. Chem. Soc., **51**, 1227 (1929).

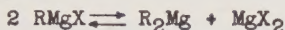
⁴A. H. Blatt and J. F. Stone, Jr., J. Am. Chem. Soc., **54**, 1495 (1932).

⁵F. F. Blicke and L. D. Powers, J. Am. Chem. Soc., **51**, 3378 (1929).

⁶M. S. Kharasch and S. Weinhouse, *op. cit.*

⁷K. Hess and H. Rheinbolt, Ber., **54**, 2043 (1921).

rated hydrocarbon and rearrange to give the reduction compound. Such a mechanism offers no explanation of the varying extents of the reduction with different alkyl magnesium halides or different ketones. Attempting to find some explanation on the basis of this mechanism, Noller and Hilmer⁸ considered that the relative reducing activity of the Grignard reagents, in such a case, should be directly related to the tendency of the corresponding alkyl halides to form alkenes, but they found no indication of such a relationship. Also, since evidence^{9,10} had been reported for the existence of the equilibrium



they studied the influence of the amount of dialkyl magnesium present, calculated upon the percentage reduction observed, but found that although the amount of benzhydrol formed from the action of a number of Grignard reagents on benzophenone increased with increasing dialkyl content of the solution, the two factors were not proportional.

Blicke and Powers¹¹ grant the possibility of the existence of the intermediate compound, but have suggested that the reaction may take place as the result of dissociation into free radicals, followed by addition to give the normal product, mutual oxidation and reduction with the formation of the reduction product, or polymerization and formation of ketones. Evidence for this type of mechanism, however, is confined to reagents of the triaryl methyl type,¹² which have been shown to dissociate into free radicals and to reduce benzophenone to benzpinacol.¹³ No pinacol formation has been reported with aliphatic Grignard reagents when the solutions were filtered, and Kharasch and Weinhouse¹⁴ have demonstrated that the absence of pinacol cannot be accounted for on the basis of rapid interaction between the Grignard reagent and the halomagnesium pinacolate to form the secondary

⁸C. R. Noller and F. B. Hilmer, J. Am. Chem. Soc., **54**, 2503 (1932).

⁹H. Gilman and R. E. Fothergill, J. Am. Chem. Soc., **51**, 3149 (1929).

¹⁰W. Schlenk and W. Schlenk, Jr., Ber., **62**, 920 (1929).

¹¹F. F. Blicke and L. D. Powers, op. cit.

¹²H. Gilman and R. E. Fothergill, op. cit.

¹³W. E. Bachmann, J. Am. Chem. Soc., **53**, 2738 (1931).

¹⁴M. S. Kharasch and S. Weinhouse, op. cit.

carbinol.

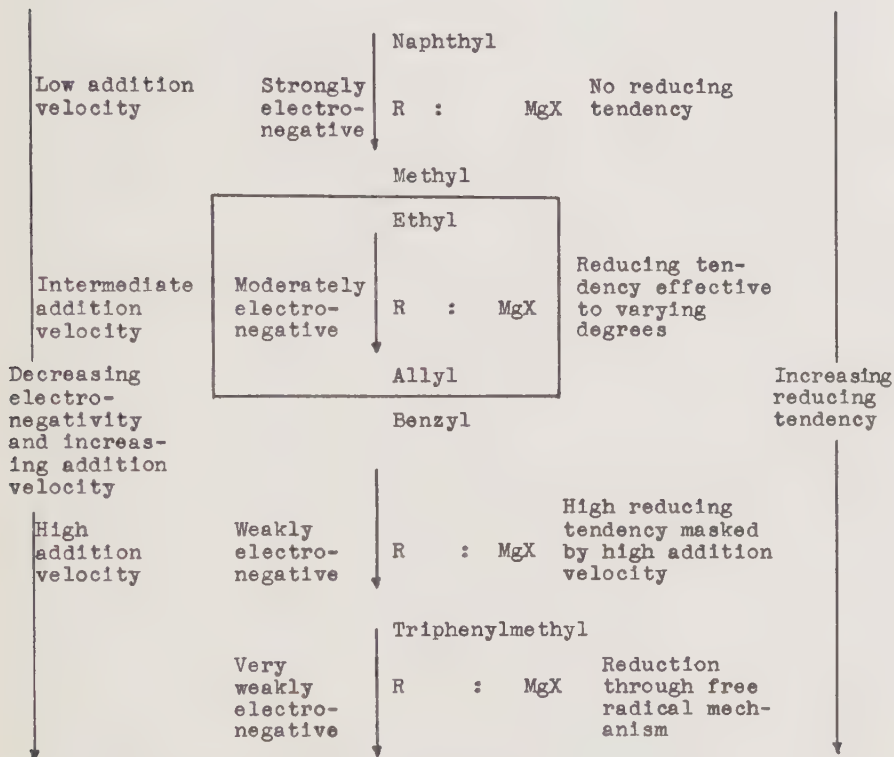
From his study of the effect of branching of chains both in the reagent and in the ketone, Conant¹⁵ concluded that there is a definite relationship between structure and reducing activity, and suggested that the reduction process is slow and occurs only when the normal addition reaction is hindered. Kharasch and Weinhouse,¹⁶ however, have demonstrated that many reduction reactions are fast, almost instantaneous, in fact, and some addition reactions are slow. These investigators have proposed a mechanism which takes this fact into consideration, and also demonstrates how the structure of the ketone may play a part in the reaction. The Grignard reagent is pictured as dissociating into a positive halomagnesium ion and a negative organic ion, which may lead either to the normal addition reaction, or, if this is hindered in some way, to reduction through the stabilization of the organic radical by the loss of two electrons to the acceptor molecule. If this mechanism is correct, the affinity of the organic radical for electrons must bear some relationship to its reducing activity, and, similarly, the electronegativity of the carbonyl carbon atom in the acceptor molecule must also have its effect upon the amount of reduction which takes place. That such a relationship does exist in the case of the Grignard reagent was fully demonstrated by these authors, who found that the reducing activity of the compound $RMgX$ increases with decreasing electronegativity of the radical R , but that this activity is masked, when R is weakly electronegative, by an increased addition velocity. When R is weakly electronegative, of the triaryl methyl type, dissociation into free radicals takes place and the product of the reduction is a pinacol. These relationships were presented graphically as shown in figure 1.

¹⁵J. B. Conant, op. cit.

¹⁶M. S. Kharasch and S. Weinhouse, op. cit.

FIGURE 1¹⁷

SCHEMATIC CORRELATION OF RADICAL ELECTRONEGATIVITIES WITH ADDITION REDUCTION TENDENCIES OF GRIGNARD REAGENTS AS EXHIBITED TOWARD BENZOPHENONE



¹⁷ M. S. Kharasch and S. Weinhouse, op. cit.

PLAN OF PROCEDURE AND DISCUSSION OF RESULTS

Since the boundaries are so clearly defined for the Grignard reagent, the next point of interest is the effect of the ketone in the reaction.

Isobutyl magnesium bromide, which gives a ninety-one per cent yield of the reduction product with benzophenone, was selected as the Grignard reagent to be used, and the percentage reduction resulting from its action upon a series of ketones was determined. As was pointed out above, the method of isolating the products is not entirely satisfactory for this purpose, and therefore it was necessary to find a less direct but more accurate method. After a considerable amount of preliminary experimentation it was found that analyzing for the secondary carbinol with acetic anhydride in pyridine solution gave consistent accurate results and this method was adopted and used throughout this investigation. In order that the results might be comparable, the amount of reduction in all cases was calculated on the basis of the amount of ketone reacting. The unreacted ketone was isolated as the 2,4-dinitrophenylhydrazone by the method of Ferrante and Bloom,¹⁸ which was found to give excellent results both with pure ketones and with mixtures of ketone and secondary carbinol. The results of this work are given in Table 1.

TABLE 1
THE RELATIVE REDUCTION OF KETONES BY
ISOBUTYLMAGNESIUMBROMIDE

Ketone	Reduction Percentage
p,p'-dichlorobenzophenone	93
Benzophenone	91
Fluorenone	51
Acetophenone	41
p,p'-dianisyl ketone	17
p,p'-ditolyl ketone	16

Although the list of ketones is not extensive, a relation-

¹⁸J. Ferrante and A. Bloom, Am. Jour. Pharm., 105, 381 (1933).

ship is immediately apparent. Dianisyl and ditolyl ketones, in which the groups attached to the carbonyl compound are more strongly electronegative than the phenyl groups in benzophenone, are reduced to a far less extent than benzophenone, and dichlorobenzophenone, in which the groups are somewhat less electronegative than phenyl, is reduced slightly more than benzophenone. This is quite in accordance with the theory of the mechanism proposed by Kharasch and Weinhouse, for it is known that strongly electronegative groups attached to a carbon atom weaken the electronegativity of that atom, and it is to be expected that the less the affinity for electrons of the carbonyl carbon atom in the acceptor molecule, the smaller should be the amount of reduction taking place with a given Grignard reagent.

The results shown in Table 1 bring out another interesting point, namely that the difference in magnitude of the effect of a methyl and methoxy substituent, large in the case of a phenyl group, is no longer apparent when transmitted through the ring to the carbonyl carbon atom of the substituted benzophenones. This diminution of effect through transmission is also seen to be true of the chlorine substituent, which is known to have a strong deactivating effect upon the phenyl group, but which has a negligible effect upon the carbonyl carbon atom. It is not intended to imply that a chlorine substituent has no influence when its effect is transmitted through the ring, nor that the transmitted effect of a methyl substituent is identical with that of a methoxy group, for the accuracy of the determinations by no means warrants such a conclusion. However, it is evident that the effect of the substituents is diminished through transmission. Also, there can be no doubt that methyl and methoxy substituents are in an entirely different class from the chlor-substituent.

Acetophenone is an anomaly in the table and is not strictly comparable to the other ketones because of the presence of the aliphatic group, through which enolization and condensation may take place. Fluorenone is of interest because of its structure; its activity must be influenced not only by the two six-membered rings, but also by the five-membered ring. That the activity of the hydrocarbon is not the same as that of diphenyl methane was shown by J. McNab¹⁹ in a study of exchange reactions in deuterio

¹⁹J. McNab, Ph.D. thesis, University of Chicago (1936).

alcohol. No exchange was observed with either compound in deuterio alcohol alone, but in the presence of 0.02 M. NaOH two hydrogen atoms in fluorene were exchanged. The cyclopentyl group, therefore, has an activating effect upon the two hydrogen atoms. The difference in the two ketones is seen in the above table which shows benzophenone to be reduced ninety-one per cent, while fluorenone is reduced only to the extent of fifty-one per cent.

It is evident that the work presented here is only a beginning, but the direction is clearly defined. With the method established, there should be no difficulty in determining the relationship between the structure of the ketone and the percentage reduction by Grignard reagents.

EXPERIMENTAL PART

THE PREPARATION OF THE GRIGNARD REAGENT

The Grignard reagent was prepared according to the method described by Kharasch and Weinhouse,²⁰ and was filtered through the sintered glass plate by gentle suction applied to an outlet in the lower flask; care was taken to exclude moisture. The reagent was standardized by the method of Gilman;²¹ a 2 cc. portion was taken for titration. Except where otherwise indicated, a ten per cent excess of isobutylmagnesium bromide was used. This was placed in a three-neck flask fitted with an air-tight mechanical stirrer, a condenser and a dropping funnel, and a solution of the ketone in dry benzene was added dropwise with stirring. During the addition, the flask was surrounded by a bucket of ice water, but after the addition was complete the reaction mixture was allowed to come to room temperature and was stirred for varying periods of time. In some cases a white precipitate formed during the reaction, but this was not separated. The mixture was hydrolyzed with dilute acid, the ether portion separated and the water layer extracted three times with ether. The combined ether extracts were then washed with Na_2CO_3 solution and finally with water until the washings were neutral to litmus, and dried over anhydrous Na_2SO_4 . The ether solution was then decanted into a weighed Erlenmeyer flask and the solvent evaporated. The residue was dried to constant weight in a vacuum desiccator, and then carefully washed into a volumetric flask with dry ether and the solution made up to 250 cc. The Erlenmeyer flask was dried and reweighed. Portions of this ether solution were used for analysis.

THE ANALYSIS FOR SECONDARY CARBINOL

The method of analysis is a modification of that used by Freed and Wynn.²² The reagent, 12 per cent acetic anhydride in

²⁰M. S. Kharasch and S. Weinhouse, op. cit.

²¹H. Gilman, E. A. Zoelner, and J. B. Dickey, J. Am. Chem. Soc., **51**, 1576 (1929).

²²M. Freed and A. M. Wynn, Ind. Eng. Chem. Anal. Ed., **8**, 278 (1936).

pyridine solution, was made from freshly distilled acetic anhydride, and pyridine which had been refluxed over barium oxide and then distilled. Portions of the ether solution of the products were pipetted into two pyrex test tubes and the solvent evaporated by drawing air over the surface. The size of the portion was determined by the weight of the products and was regulated so that a 100 per cent yield of secondary carbinol would require no more than one-fourth of the titratable acidity of the reagent. To one of the tubes was added a weighed amount of secondary carbinol, and to each of the tubes exactly 2 cc. of a 12 per cent solution of acetic anhydride in pyridine. A glass bead was dropped into each tube to prevent bumping, and the tubes were fitted with "finger" condensers, which were found to be extremely efficient. The solutions were refluxed over micro-burners for one hour, allowed to cool, and then washed into Erlenmeyer flasks in the following manner: 5 cc. of carbon dioxide-free water was added directly to each tube and the contents poured into the flask; the sides of the condenser and the tube were then washed with two 10 cc. portions of water and finally with one 10 cc. portion of alcohol. The samples were titrated with 0.1 N. NaOH, using phenolphthalein as indicator. Blanks were run on the reagent. The difference in titre between the blank and the sample represents the number of millimols of secondary carbinol in the sample. The wash alcohol as used was shown to have no effect on the results.

THE ANALYSIS FOR KETONE

The reagent was prepared according to the directions of Ferrante and Bloom:²³ 2 gm. of 2,4-dinitrophenylhydrazine was dissolved in 5 cc. of concentrated H_2SO_4 and the solution was made up to 50 cc. with methyl alcohol.

Method.--A sample of the ether solution of the product from the Grignard reaction was pipetted into a 125 cc. Erlenmeyer flask and the solvent evaporated. To this were added 10 cc. of methyl alcohol and a sufficient quantity of the reagent so that the 2,4-dinitrophenylhydrazine was in excess of the possible amount of the ketone present; this was calculated on the basis that all the product not accounted for as secondary carbinol was ketone. The size of the original sample of ether solution was

²³ J. Ferrante and A. Bloom, op. cit.

determined by the amount of secondary carbinol previously found. After addition of the reagent, the flask was swirled vigorously until the precipitate which formed began to settle, and the mixture was allowed to stand overnight. It was then filtered through a weighed sintered glass funnel, and the precipitate was washed with 10 cc. of methyl alcohol to which two drops of concentrated H_2SO_4 had been added, and finally with 2.5 cc. of methyl alcohol. The funnel was placed in a drying oven at 80° for forty-five minutes and then in a vacuum desiccator over P_2O_5 until it reached constant weight.

STANDARDIZATION OF THE METHODS

Samples of carbinol were analyzed in the manner described above to determine the accuracy of the method. The results are summarized in Table 2.

TABLE 2
ANALYSIS FOR SECONDARY CARBINOL WITH ACETIC ANHYDRIDE AND PYRIDINE

Carbinol	Weight of Sample Gm.	Difference in Titre cc. NaOH	Normality NaOH	Carbinol Found	
				Gm.	Per Cent
Diphenyl ethyl carbinol.	0.0527	0.02	0.1000	0.000	0.0
Benzhydrol.....	0.2115	11.41	0.0987	0.2072	98.0
Benzhydrol.....	0.2379	12.67	0.0987	0.2302	96.8
p,p'-dimethoxybenzhydrol	0.2093	8.46	0.0987	0.2038	97.5
Fluorenol.....	0.2141	11.58	0.0987	0.2080	97.2
p,p'-dimethylbenzhydrol.	0.0794	3.87	0.0942	0.0773	97.4
p,p'-dimethylbenzhydrol.	0.1070	5.26	0.0942	0.1051	98.2
p,p'-dichlorobenzhydrol.	0.0506	2.22	0.0942	0.0529	104.5
p,p'-dichlorobenzhydrol.	0.0431	1.84	0.0942	0.0439	101.7
Phenyl methyl carbinol..	0.1166	8.49	0.0942	0.0976	83.7
Phenyl methyl carbinol..	0.1070	7.77	0.0942	0.0893	83.5
Phenyl methyl carbinol ^a .	0.1088	7.79	0.0942	0.0895	82.3
Phenyl methyl carbinol ^a .	0.1059	7.71	0.0942	0.0886	83.7
Phenyl methyl carbonol ^b .	0.0948	6.79	0.0942	0.0781	82.4
Phenyl methyl carbinol ^b .	0.1166	8.19	0.0942	0.0941	80.7

^aCarbinol redistilled under reduced pressure.

^bCarbinol washed three times with saturated $NaHSO_3$ and redistilled.

Mixtures of benzhydrol and diphenyl ethyl carbinol were analyzed by the same method. The results are summarized in Table 3.

Analysis for ketone.--To 0.1901 gm. of p,p'-dianisyl ketone were added 10 cc. of methyl alcohol, 1.5 gm. of benzhydrol,

TABLE 3
ANALYSES OF MIXTURES OF BENZHYDROL AND DIPHENYL ETHYL
CARBINOL WITH ACETIC ANHYDRIDE IN PYRIDINE

Tert. Carbinol Gm.	Benz- hydrol Gm.	Secondary Carbinol in Mixture Wt.Per Cent	Differ- ence in Titre cc.	Nor- mality NaOH	Benz- hydrol Gm.	Benzhydrol Found in Mixture Wt.Per Cent
0.3896	0.0457	10.5	2.45	0.1000	0.0451	10.4
0.4113	0.0474	10.3	2.52	0.1000	0.0464	10.1
0.1238	0.0734	37.2	3.98	0.1000	0.0732	37.1

and 5 cc. of the 2,4-dinitrophenylhydrazine reagent. The procedure was that described above. Yield: 0.3277 gm. (calc. 0.3303 gm.), 99.2% of calc., m. pt. 194-196°.

Analysis:²⁴ Calc. for $C_{21}H_{18}O_6N_4$: N, 13.27%

Found: N, 13.60%

A sample of benzophenone weighing 0.1657 gm. was dissolved in 15 cc. of methyl alcohol, and to this were added 1.5 gm. benzhydrol and 10 cc. of reagent. Yield: 0.3374 gm. (102% of calc.), m. pt. 230°. A second determination was run in which 0.1963 gm. of benzophenone, 1.5 gm. of benzhydrol, and 10 cc. of methyl alcohol were used. Yield: 0.3871 gm. (99.1% of calc.), m. pt. 230°. To 0.2104 gm. of acetophenone and 1.5 gm. benzhydrol in 15 cc. of methyl alcohol was added 10 cc. of reagent. Yield: 0.5285 gm. (100.4% of calc.), m. pt. 237°. Analysis for fluorenone by this method was not so satisfactory. To 0.1684 gm. of the ketone and 1.5 gm. of benzhydrol dissolved in 20 cc. of methyl alcohol was added 5 cc. of the reagent. Yield: 0.2821 gm. (84% of calc.), m. pt. 291-292°. The 2,4-dinitrophenylhydrazone of fluorenone previously prepared in glacial acetic acid melted sharply at 300°. A second determination was made using 10 cc. of methyl alcohol, 0.1402 gm. of ketone, 1.5 gm. benzhydrol, and 5 cc. of reagent. Yield: 0.2488 gm. (88% of calc.). To 0.1923 gm. of p,p'-ditolyl ketone and 1.5 gm. of benzhydrol in 10 cc. of methyl alcohol was added 5 cc. of the reagent. Yield: 0.3531 gm. (99% of calc.), m. pt. 210-212°. The procedure was varied in a second determination, since it was found that a small amount of material in the product from the Grignard reaction was insoluble in the amount of

²⁴The author wishes to express her gratitude to Mr. K. Eder for the nitrogen analyses presented in this paper.

methyl alcohol usually employed, but was completely soluble in an ether-methyl alcohol mixture. A solution of 0.1552 gm. of p,p'-ditolyl ketone, and 1.2 gm. of benzhydrol in 10 cc. of methyl alcohol was treated with 10 cc. of the reagent. Yield: 0.2845 gm. (98.7% of calc.), m. pt. 212-213°. The reported melting point of the 2,4-dinitrophenylhydrazone is 229.4°. Repeated washing with methyl alcohol of the product described above, however, failed to raise the melting point more than two degrees.

Analysis: Calc. for $C_{21}H_{18}O_4N_4$: N, 14.36%,

Found: N, 14.20%.

With p,p'-dichlorobenzophenone, the usual procedure was followed. To a solution of 0.1221 gm. of ketone, and 1.5 gm. benzhydrol in 15 cc. of methyl alcohol was added 5 cc. of the reagent. Yield: 0.2052 gm. (97.9% of calc.), m. pt. 229°.

Analysis: Calc. for $C_{19}H_{12}O_4Cl_2N_4$: N, 12.99%,

Found: N, 13.36%.

EXPERIMENTAL RESULTS

ACTION OF ISOBUTYL MAGNESIUM BROMIDE ON BENZOPHENONE

To 25 cc. of 1.66 N. isobutyl magnesium bromide was added dropwise, with stirring, a solution of 6.40 gm. benzophenone in 15 cc. of dry benzene. After addition was complete, the mixture was allowed to stand at room temperature for one hour and 15 minutes, and was then hydrolyzed with dilute H_2SO_4 . The product, 6.6652 gm., was prepared for analysis by the procedure which has already been described.

Analysis for secondary carbinol.--Into each of two test tubes was pipetted 5 cc. of the ether solution of the product, and to one tube was added, after evaporation of the solvent, 0.0202 gm. of benzhydrol. To each tube was added exactly 2 cc. of acetic anhydride-pyridine reagent, and the solutions were treated in the usual manner. Titrations were carried out with 0.1000 N. NaOH. The results are tabulated below.

Analysis for ketone.--The solvent was evaporated from a 25 cc. portion of the ether solution of the product, (0.6665 gm.), and 5 cc. of the 2,4-dinitrophenylhydrazine reagent and 10 cc. of methyl alcohol were added. Yield: 0.0971 gm. (7.3% of calc.), m. pt. 230-231°.

Sample	Difference in Titre cc.	Secondary Carbinol Found Gm.	Secondary Car- binol Found Minus Car- binol Added	Secondary Carbinol Per Cent	Carbinol in Total Product Gm.
0.1333 gm. of product	5.95	0.1095	0.1095	82	5.46
0.1333 gm. product + 0.0202 gm. benzhydrol	7.05	0.1297	0.1095	82	5.46

ACTION OF ISOBUTYL MAGNESIUM
BROMIDE ON FLUORENONE

A solution of 5.40 gm. of fluorenone in 15 cc. of dry benzene was added to 21 cc. of a 1.66 N. solution of isobutyl magnesium bromide. After addition was complete, the mixture was stirred for one hour at room temperature. Yield: 6.5052 gm.

Analysis for secondary carbinol.--Determinations made on two 5 cc. samples of the ether solution containing 0.1301 gm. of product each, gave the following results:

Sample	Difference in Titre cc. 0.1000 N. NaOH	Secondary Carbinol Found Gm.	Secondary Carbinol in Sample of Product Gm.	Secondary Carbinol in Product Per Cent	Secondary Carbinol in Total Product Gm.
0.1301 gm. product	3.15	0.0573	0.0573	44.0	2.86
0.1301 gm. product + 0.0203 gm. fluoreno ^a	4.00	0.0728	0.0539	41.4	2.69

^aAnalyzed 92%.

Analysis for ketone, using 10 cc. of the ether solution of the product, 10 cc. of methyl alcohol, and 5 cc. of the reagent, yielded only a small amount of precipitate which decomposed in the desiccator.

ACTION OF ISOBUTYL MAGNESIUM
BROMIDE ON ACETOPHENONE

To 30 cc. of a 1.60 N. solution of the Grignard reagent was added with stirring, 4.80 gm. of acetophenone in 10 cc. of dry benzene. The solution was stirred for one hour after all the

ketone had been added, and was hydrolyzed with dilute HCl. After the usual treatment, a reddish oil was obtained, which, contrary to custom, was not dissolved in ether, but was used directly in the analysis. Yield: 5.0597 gm.

Analysis for secondary carbinol.--Determinations made on the weighed samples of the product gave the following results:

Sample	Difference in Titre cc. 0.0942 N. NaOH	Secondary Carbinol Found Gm.	Secondary Carbinol in Sample of Product Gm.	Secondary Carbinol in Product Per Cent	Secondary Carbinol in Total Product Gm.
0.1300 gm. product	4.04	0.0464	0.0464	35.7	1.81
0.1022 gm. product + 0.0978 gm. phenyl meth- yl carb. ^a	10.17	0.1169	0.0364	35.6 ^b	1.80

^aAnalyzed 82%.

^bCalculated on the basis that 0.0364 gm. represents the total secondary carbinol in the sample.

Analysis for ketone.--In the analysis of the product for unreacted ketone, 0.1677 gm. of the oil was dissolved in 10 cc. of methyl alcohol and 10 cc. of the reagent was added. Yield of 2,4-dinitrophenylhydrazones: 0.0386 gm. (9.2% of value calc. for 100% ketone), m. pt. 235-237°. This corresponds to 0.466 gm. of unreacted ketone in the total product.

ACTION OF ISOBUTYL MAGNESIUM BROMIDE ON P,P'-DIMETHOXYBENZOPHENONE

To 21 cc. of a 1.60 N. solution of the Grignard reagent was added at room temperature, a solution of 4.85 gm. of p,p'-dimethoxybenzophenone in 100 cc. of warm, dry benzene. The addition was fairly rapid because the ketone precipitated out of the solution if it was allowed to drop in slowly. The mixture was stirred for twenty hours, after which it was hydrolyzed with dilute HCl, and then treated in the customary manner. Yield: 5.4077 gm.

Analysis for secondary carbinol.--Analysis of two 5 cc. samples, to one of which had been added 0.0487 gm. of p,p'-dimethoxybenzhydrol, gave the following results:

Sample	Difference in Titre cc. 0.0942 N. NaOH	Secondary Carbinol Found Gm.	Secondary Carbinol in Sample of Product Gm.	Secondary Carbinol in Product Per Cent	Secondary Carbinol in Product Gm.
0.1082 gm. product	0.61	0.0139	0.0139	12.8	0.692
0.1082 gm. product + 0.0487 gm. hydrol	2.69	0.0618	0.0131	12.1	0.654

Analysis for ketone.--The ether was evaporated from 10 cc. of the solution of the product from the Grignard reaction and to this were added 10 cc. of methyl alcohol and 5 cc. of the 2,4-dinitrophenylhydrazine reagent. Yield: 0.0529 gm. (14% of value calc. for 100% ketone), m. pt. 192-200°. The total unreacted ketone, therefore, in the original product from the Grignard reaction was 0.757 gm.

ACTION OF ISOBUTYL MAGNESIUM
BROMIDE ON P,P'-DITOLYL KETONE

To 20 cc. of a 1.85 N. solution of isobutyl magnesium bromide was added dropwise, a solution of 6.30 gm. of p,p'-ditolyl ketone in 10 cc. of dry ether and 10 cc. of dry benzene, and the mixture was stirred for two hours after the addition was complete, and then hydrolyzed with dilute H₂SO₄. Yield: 6.3528 gm.

Analysis for secondary carbinol.--A summary of the analyses of the 10 cc. samples of the ether solution of the product is given below.

Sample	Difference in Titre cc. 0.0942 N. NaOH	Secondary Carbinol Found Gm.	Secondary Carbinol in Sample of Product Gm.	Secondary Carbinol in Product Per Cent	Secondary Carbinol in Total Product Gm.
0.2541 gm. product	1.32	0.0263	0.0263	10.4	0.660
0.2541 gm. product + 0.0393 gm. ditolyl carb. (92%)	3.08	0.0615	0.0254	10.0	0.635

Analysis for ketone.--To 10 cc. of the ether solution were added directly, without evaporation of solvent, 10 cc. of methyl alcohol and 10 cc. of the reagent. Yield of 2,4-dinitro-phenylhydrazone: 0.1652 gm. (35% of value calc. for 100% ketone). The total unreacted ketone in the original product from the Grignard reaction was therefore 2.22 gm.

ACTION OF ISOBUTYL MAGNESIUM BROMIDE ON P,P'-DICHLOROBENZOPHENONE

To 13 cc. of 1.85 N. solution of isobutyl magnesium bromide was added 5.02 gm. of p,p'-dichlorobenzophenone in 50 cc. of warm, dry benzene. The violet color at first formed, changed to a light amber. The mixture was allowed to react over night and was then hydrolyzed with dilute HCl. Yield: 4.9786 gm.

Analysis for secondary carbinol.--In the analyses, 10 cc. samples were used. The procedure was varied slightly in that acetone instead of ethyl alcohol was used for rinsing the tubes, because of the presence of a large amount of material insoluble in alcohol. The results are summarized below.

Sample	Difference in Titre cc. 0.0942 N. NaOH	Secondary Carbinol Found Gm.	Secondary Carbinol in Sample of Product Gm.	Secondary Carbinol in Product Per Cent	Secondary Carbinol in Total Product Gm.
0.1991 gm. product	3.88	0.0925	0.0925	46.5	2.34
0.1991 gm. product + 0.0796 gm. hydro(103%)	7.42	0.1768	0.0948	47.6	2.37

Analysis for ketone.--To a 10 cc. sample of the ether solution containing 0.1991 gm. of product, were added after the evaporation of the solvent, 10 cc. of methyl alcohol and 5 cc. of the reagent. Yield of 2,4-dinitrophenylhydrazone: 0.1721 gm. (50.4% of the value calc. for 100% ketone), m. pt. 230-231°. This is equivalent to 2.505 gm. of unreacted ketone in the original product from the Grignard reaction.

A summary of the experimental results is presented in Table 4.

TABLE 4

THE ACTION OF ISOBUTYL MAGNESIUM BROMIDE ON VARIOUS KETONES

Compound	Ketone Added Gm.	Product Gm.	Sec. Butinol in Product Gm.	Unreacted Ketone Gm.	Reduction Per Cent
Benzophenone	6.40	6.67	5.46	0.49	91
Fluorenone	5.40	6.51	2.78		51
Acetophenone	4.80	5.06	1.81	0.43	41
p,p'-dichloro- benzophenone	5.02	4.98	2.34	2.51	95
p,p'-ditolyl ketone	6.30	6.35	0.69	2.22	17
p,p'-dianisyl ketone	4.85	5.41	0.67	0.76	16

SUMMARY

1. A method has been developed for the determination of the amount of secondary aromatic carbinol in a mixture of secondary and tertiary carbinols.

2. The relative reducing action of isobutyl magnesium bromide on a number of ketones has been studied. The ketones included benzophenone, p,p'-dichlorobenzophenone, fluorenone, acetophenone, p,p'-ditolyl ketone, and p,p'-dimethoxybenzophenone. The results indicate that in a substituted benzophenone, the amount of reduction taking place depends upon the relative electronegativity of the groups attached to the carbonyl group; the more electronegative the group, the less the reduction.

3. Benzophenone and dichlorobenzophenone are reduced to approximately the same extent by isobutylmagnesiumbromide, 91% and 93% respectively. Similarly, p,p'-ditolyl ketone is reduced by the same reagent to the same extent as p,p'-dianisyl ketone, 16% and 17% respectively.

